REMARKS

Status of the Claims

Claims 1-28 are pending, and elected claims 1-2, 4, 8, 15-16, and 20 should be examined. Claim 20 is amended. No new matter has been added.

Response to Restriction Requirement

In a response filed July 25, 2003, applicants responded to a restriction by electing "Group I" claims 1-2, 4, 8, 15-16, and 20. In the Office Action of November 14, 2003, the examiner indicated that the elected claims will be examined only to the extent that they embrace "methods for transforming fungal and animal cells." See Office Action, page 2. Applicants respectfully traverse this imposed claim limitation.

Where only generic claims are presented, no restriction can be required except in those applications where the generic claims recite such a multiplicity of species that an unduly extensive and burdensome search is necessary. MPEP § 809.02(d).

Here, claim 1 is drawn to a method for producing an oil body associated with a recombinant multimeric-protein-complex in a cell comprising oil bodies. As indicated in the specification, oil bodies may be obtained from any cell comprising oil bodies, including plant cells, animal cells, algae cells, fungal cells, and bacterial cells. See specification, at page 24, lines 3-16. Accordingly, the specification discloses oil bodies from several cell types. Yet the examiner has indicated that claim term "cell" will be examined as if it were limited to fungal and animal cells.

The record presents no rationale for a species election. Since there is no serious or extensive burden upon the examiner, the apparent species election is improper here and should be withdrawn. Procedurally, moreover, applicants would have to make any such election; the examiner cannot do so for the applicant. MPEP § 818.03(e). For at least these reasons, applicants respectfully submit that the restriction requirement is in error and request that the requirement be withdrawn.

Response to Double Patenting Rejection

Claims 1-2, 4, 8, 15-16, and 20 stand rejected over claims 1, 10-11, 14-16, and 19-20 of U.S. Patent No. 5,948,682 ("the '682 patent"). The examiner alleges that, while the present claims are not identical to those of the '682 patent, it would have been obvious to utilize methodology recited in the latter claims to obtain a fusion protein comprised of an oil body protein and a thioredoxin or thioredoxin reductase protein. See Office Action, page 3. Applicants respectfully traverse this rejection.

According to MPEP § 804, a proper analysis in this context must parallel the guidelines set forth for an obviousness rejection under Section 103. Specifically, the examiner has the burden for establishing *why* the skilled artisan would have deemed the invention of the subject claim as an obvious variation on the invention recited in the claim of a patent.

Yet the record offers up no basis for reaching the presently claimed invention, absent impermissible hindsight, from the vantage of the methodology claimed in the '682 patent. In particular, the examiner has identified no evidence of motivation in the art to have modified the latter methodology to achieve applicants' claimed invention. For these reasons alone, the rejection is improper and should be withdrawn.

Furthermore, the methods of the '682 patent actually cannot be employed to reach the claimed invention. That is, the '682 patent claims would not have led the person of ordinary skill to the claimed "method for producing an oil body associated with a recombinant multimeric-protein-complex."

Specifically, the '682 patent describes using an oil body protein gene for targeting a heterologous polypeptide as a fusion protein to an oil body. In other words, the '682 patent provides a means to express a single polypeptide on an oil body. Conversely, the present invention discloses a means to associate a multimeric protein complex with an oil body. Thus, the present invention discloses a method for associating an oil body with at least two polypeptides, by any means, that permanently or repeatedly interact or coordinate to form a biologically active assembly.

Accordingly, the '682 patent neither provides guidance for nor evidences motivation by one of ordinary skill for associating an oil body with a multimeric protein complex, let alone a thioredoxin/thioredoxin reductase protein complex. The rejection therefore is improper and should be withdrawn.

Rejections under 35 U.S.C. § 112, second paragraph

The examiner has rejected claim 20 for alleged indefiniteness. See Office Action, page 3. Since his stated concern is inapposite to the present claim, however, the rejection should be withdrawn.

Rejections under 35 U.S.C. § 112, first paragraph (written description)

Under this rubric there are several rejections relating to claims 1-2, 4, 8, 15-16, and 20, and each rejection is addressed below.

The examiner alleges that the specification does not provide guidance for "isolation of other thioredoxin enzymes, such as ferredoxin reductase." Office Action, page 4. As ferredoxin reductase reduces ferredoxin, ferredoxin reductase is not a thioredoxin. Thus, applicants do not need to provide guidance for the isolation of a ferredoxin reductase. Accordingly, the rejection should be withdrawn.

Applicants respectfully submit that specification provides guidance for the isolation of thioredoxin genes or thioredoxin reductase genes. In particular, the specification discloses exemplary nucleic acid sequences for thioredoxin. For example, see pages 44-45, SEQ ID NOs 38, 42, 46 and 50 , and Table 5. Furthermore, exemplary nucleic acid sequences encoding thioredoxin reductases are also provided. For instance, see SEQ ID Nos 8, 9 10, 40, 44, 28 and 50, and SEQ ID NOs 195-313 (Table 5). The specification also provides guidance for isolating nucleic and amino acid sequences that are "substantially homologous" to the thioredoxin and thioredoxin-reductase nucleic and amino acids set forth in the application, which includes thioredoxin and thioredoxin-reductase polypeptides encoded by a sequence of nucleotides that hybridize under conditions of low, moderate or high stringency to the sequence of nucleotides encoding the thioredoxin and thioredoxin-reductase. See, for example, page 46, lines 2-page 49, line 25.

It also is alleged that the specification does not provide guidance for "isolation or characterization of a multitude of fragments of any size and sequence from a multitude of thioredoxin genes or thioredoxin reductase genes." Office Action, page 4. Applicants respectfully traverse this ground for rejection.

As described above, the specification discloses exemplary nucleic acid sequences for thioredoxin. For example, see pages 44-45, SEQ ID NOs 38, 42, 46 and 50, and Table 5. Furthermore, exemplary nucleic acid sequences encoding thioredoxin reductases are also provided. For instance, see SEQ ID Nos 8, 9 10, 40, 44, 28 and 50, and SEQ ID NOs 195-313 (Table 5). The specification also provides guidance for isolating nucleic and amino acid sequences that are "substantially homologous" to the thioredoxin and thioredoxin-reductase nucleic and amino acids set forth in the application, which includes thioredoxin and thioredoxin-reductase polypeptides and fragments encoded by a sequence of nucleotides that hybridize under conditions of low, moderate or high stringency to the sequence of nucleotides encoding the thioredoxin and thioredoxin-reductase. See, for example, page 46, lines 2-page 49, line 25. The specification also clearly sets out the active site of thioredoxin (see page 43, line 16 - page 44, line 1) and of thioredoxin reductase (see page 45, lines 2 – 8) which would be required for an active fragment of a thioredoxin-related protein. Guidance for the characterization of a thioredoxin or thioredoxin-redutase polypeptide or fragment is provided in example 4. As outlined in the example, the activity can be determined using the "DTNB assay" and the "insulin reduction assay." Finally, a person ordinarily skilled in the art would be able to create thioredoxin and thioredoxin-reductase fragments using for example the generation of deletion mutations (see for example Sambrook and Russell in: Molecular Cloning, A Laboratory Manual 3rd Edition, Cold Spring Harbor Laboratory Press (2001), vol. 3, p. 13.57-13.96),

Thus, the specification provides ample guidance for the skilled person to isolate or characterize a myriad of thioredoxin and thioredoxin-reductase nucleic acid and amino acid sequences, respectively. Therefore, the rejection is improper and should be withdrawn.

Rejections under 35 U.S.C. § 112, first paragraph (enablement)

As to claims 1-2 and 8, the examiner alleges in this regard that the specification does not enable "associating thioredoxin or thioredoxin reductase with oil body proteins." Office Action, page 6. Applicants respectfully traverse this rejection.

For a sustainable "non-enablement" rejection, the Office has "the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention." MPEP § 2164.04. The Office may do so by "making **specific** findings of fact, supported by evidence, and then drawing conclusions based on these findings of fact" ... "**specific** technical reasons are always required." MPEP. § 2164.04 (emphasis added).

In the present instance, the examiner supports his position with a **generalized** assertion but never identifies any specific technical reasons for that position. Thus, the examiner states that, in general, "the location of heterologous proteins in transformed cells is unpredictable" (page 7), but he never discusses oil body proteins, let alone the targeting of oil body proteins. Additionally, the examiner never cites any documentation indicating that oil body targeting proteins have been misdirected.

By contrast, applicants submit that oil body proteins, such as oleosins and caleosins, have predictable and well-characterized targeting. See Lee *et al.*, *PNAS* 88:14: 6181-85 (1991), previously made of record via an IDS. Furthermore, applicants have demonstrated predictable and consistent oil body protein targeting with more than twenty-five proteins. See, for example, van Rooijen and Moloney, *Biotechnology* 13: 72-77 (1995), and Parmenter *et al.*, *Plant Molecular Biology* 29: 1167-80 (1995), likewise of record. Notably, the examiner has not mentioned these publications or, more to the point, provided any **specific** technical commentary on their content.

Furthermore, the examiner alleges that the specification does not provide any other means for associating heterologous proteins with oil bodies. Yet the specification provides several methods for interacting two or more polypeptides, including covalent and non-covalent methods. For example, the specification provides support for a non-covalent

interaction between an oil-body-targeting protein and an immunoglobulin polypeptide chain. See specification, page 24, lines 17-25. Accordingly, the specification provides several and varied methods for a skilled artisan to associate heterologous proteins with oil bodies.

For the reasons advanced, it necessarily follows that the examiner has not met his initial burden of establishing a reasonable basis to question the enablement of the claimed invention. Accordingly, applicants respectfully request withdrawal of this rejection.

Rejections under 35 U.S.C. § 102(b)

Claim 20 allegedly is anticipated by Ting *et al.* According to the examiner, Ting *et al.* discloses a nucleic acid construct comprising a yeast-expressible promoter that is ligated to a gene coding for a maize oil body protein. Moreover, the examiner alleges "an oil body protein gene would inherently contain a fragment of **at least one base pair of a thioredoxin gene or a thioredoxin reductase gene**." Office Action, page 8 (emphasis added). This rejection is improper and should be withdrawn.

According to MPEP § 2112, an anticipation rejection based on inherency must be supported by an examiner's proffered factual and technical grounds, establishing that the inherent feature *necessarily* flows from the teachings of the prior art. *Ex parte Levy*, 17 U.S.P.Q.2d 1461, 1464 (Bd. Pat. App. & Int. 1990) (emphasis added). In fact, inherency **must** flow as a necessary conclusion from the prior art, and not simply a possible one. *In re Oelrich*, 666 F.2d 578, 581, 212 U.S.P.Q. 323, 326 (C.C.P.A. 1981) (emphasis added).

Against this background, the examiner is heard to say that an oil body protein gene inherently contains a "fragment thereof," as recited, by virtue of comprising at least one base pair "of a thioredoxin gene." Yet one base pair cannot be "of" (*i.e.*, cannot be tied uniquely to) any given coding segment or gene, let alone a region encoding an active fragment of a thioredoxin-related protein, again as recited. By the same token, no oil body protein gene ***necessarily*** contains some portion that characterizes (is "of") a thioredoxin or a thioredoxin reductase gene. For this reason alone, the examiner's inherency rationale is faulty and the rejection warranting of withdrawal.

Furthermore, an anticipating reference must teach every element of the claimed invention. MPEP § 2131. If even one recited element is absent from the reference, that disclosure cannot anticipate the claim. From this perspective, Ting *et al.* cannot anticipate because its does not disclose operably linking an oil body protein to another protein, let alone to a "thioredoxin-reductase protein." For this reason, too, Ting *et al.* does not anticipate the claimed invention, and the rejection should be withdrawn.

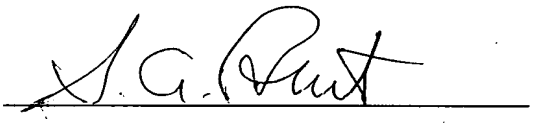
CONCLUSION

As the above-presented amendments and remarks address and avoids all of the rejections presented by the examiner, withdrawal of the rejections and allowance of the claims are respectfully requested. No new matter has been added.

If there are any questions concerning this application, the examiner is courteously invited to contact the undersigned counsel.

Respectfully submitted,

Date March 11, 2004

By 

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